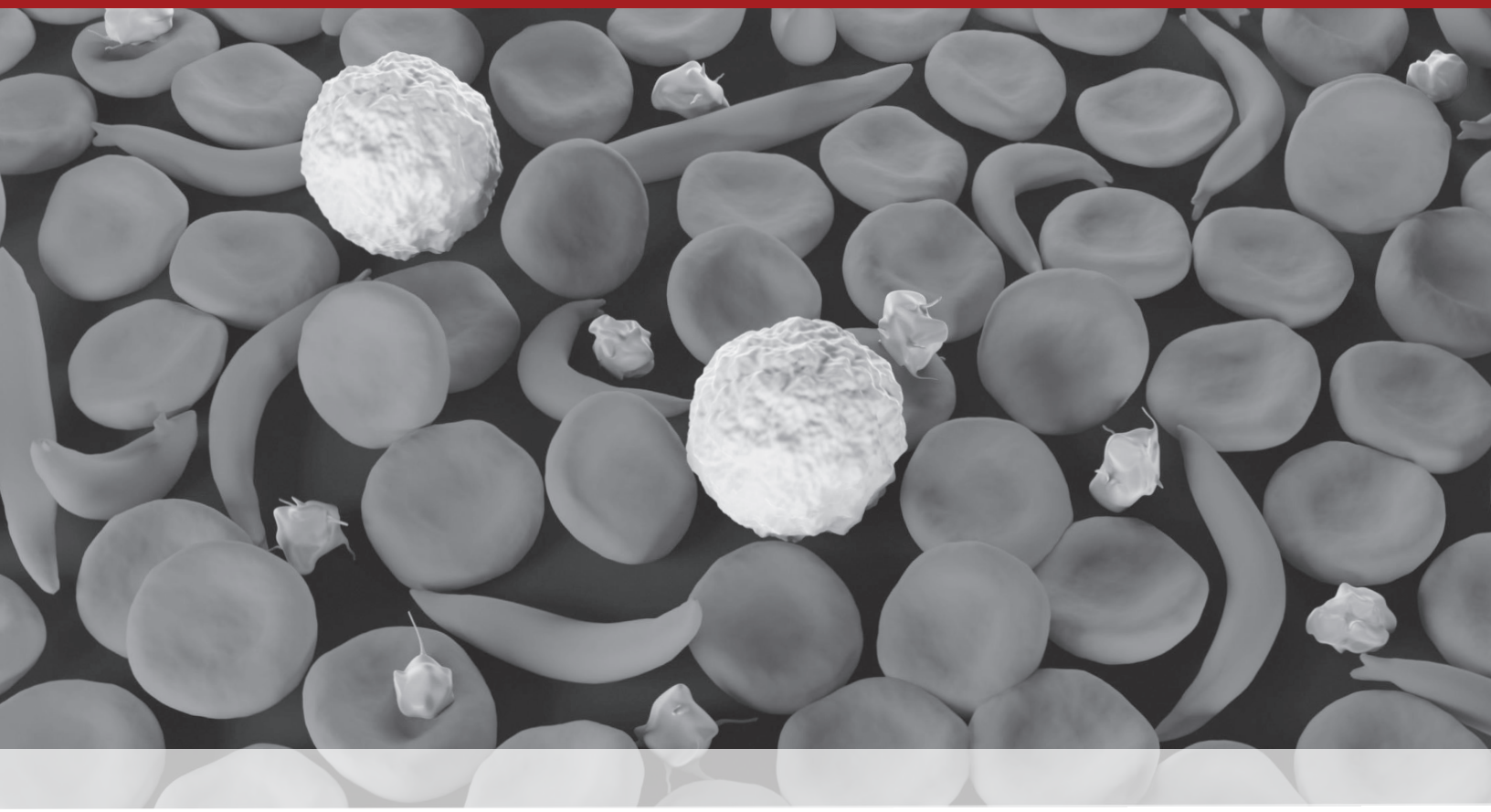
SCiF
SICKLE CELL IN FOCUS
KINGSTON • WASHINGTON

The 13th Sickle Cell in Focus Conference

October 10-11, 2019

Jamaica Pegasus Hotel
81 Knutsford Boulevard
Kingston 5, Jamaica West Indies



NIH National Heart, Lung, and Blood Institute

SCC Sickle Cell Unit UWI, Jamaica


NATIONAL INSTITUTES OF HEALTH

Hello and a very warm welcome to the 13th annual Sickle Cell in Focus (SCiF) Conference!

The National Heart, Lung, and Blood Institute (NHLBI) is excited to be co-hosting the conference with the University of West Indies once again. Historically, investigators and physicians from Asia, Europe, Brazil, Africa, and the Caribbean have participated heavily in SCiF in London and the USA. In co-hosting biannually with the University of West Indies, we continue to move towards greater collaboration with researchers and health care professionals working with sickle cell disease around the world. We will successfully expand our capacity to provide consultants, trainee doctors, healthcare professionals, and academics interested in hemoglobin disorders with an opportunity for a comprehensive exploration of current medical trends and research results in sickle cell disease globally.

During this two-day, intensive, educational update on sickle cell disease, we will focus on updates on management of commonly encountered sickle-related complications, curative therapies, and a reality check on current treatment options- blood transfusion, hydroxyurea and L-glutamine - as well as emerging genomic therapies. There will also be one debate at the end of each conference day on topical issues for which there are no clear answers. We received wonderful feedback on the quality and knowledge-level of speakers at last year's conference and are excited to have yet another great line up this year. These speakers are experts in their field and will highlight the latest in high-quality research in sickle cell disease. We thank them in advance for giving us their precious time to make SCiF successful.

We sincerely hope that you will enjoy SCiF 2019 in Kingston, Jamaica. We would like to thank you for supporting NHLBI and UWI with your attendance at SCiF; delegates are vital to the success of the conference . Your feedback is important and highly appreciated. Please keep an eye out following the event for an event evaluation form, as it helps us shape the program for next year.

Thank you to all our attendees, especially those who have travelled from overseas, for their participation in this year's conference. We hope to see you again in Bethesda, MD for Sickle Cell in Focus 2020.

Best Wishes,
Swee Lay Thein, John Tisdale, Jennifer Knight-Madden and Monika Asnani

Program Directors

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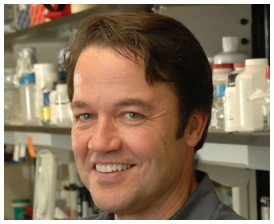

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AGENDA Day One: Thursday, October 10th 2019

8:00am **Registration**

9:00am **Welcome and Introduction**

SESSION ONE – CHAIR: Jennifer Knight-Madden – SICKLE CELL DISEASE AROUND THE WORLD

9:15am **United States of America**
Kathryn Hassell (Denver, Colorado, US)
Department of Medicine, Division of Hematology, University of Colorado Denver, USA

9:30am **The Caribbean**
M. Hardy – Dessources, Guadeloupe
UMR_S 1134, Inserm/ Université des Antilles, CHU Pointe à Pitre, Guadeloupe

9:45am **Africa**
J. Makani – Tanzania
Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania

10:00am **India**
Dipty Jain
Indira Gandhi Government Medical College and Mayo Hospital, Nagpur, India

10:15am **Europe**
Jacques Elion – France
Université Paris Diderot, Sorbonnne Paris Cité, France

10:30am **Brazil**
Fernando Costa (UNICAMP)
Cidade Universitária Zeferino Vaz, Campinas, Brazil

10:45am **Discussion**

11.00am **BREAK**

SESSION TWO – CHAIR: Angela Rankine-Mullings
CAN WE CURE AND/OR PREVENT SICKLE CELL DISEASE

11:25am **Gene Editing a nd Gene Therapy**
Punam Malik
Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

11:55am **Source of Cells – Impact on Success of BMT**
John Tisdale
National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, USA

12:15pm **Long Term Outcomes of BMT**
Matt Hsieh
National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, USA

12:35pm **LUNCH**

SESSION THREE – CHAIR: Arun Shet – DISEASE MODIFICATION OF SICKLE CELL DISEASE

1:35pm **HU Around the World – Africa, India, Caribbean, and Developed World**
Russell Ware
Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

2:05pm **Update on Clinical Trials**
Matthew Heeney
Boston Children's Hospital, Boston, MA, USA

2.35pm **Experience with L-glutamine**
Charles Quinn
Cincinnati Children's Hospital, Cincinnati, OH, USA

SESSION FOUR – CHAIR: Matt Hsieh – PROBLEMS IN MANAGING SICKLE CELL DISEASE

2:50pm **How I Manage Venous Thromboembolisms in SCD**
Arun Shet
National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, USA

3:10pm **Opioid and Marijuana in SCD**
Susanna Curtis
Yale School of Medicine, New Haven, CT, USA

3:35pm **Pain as a Complex Phenotype**
Deepika Darbari
Children's National Medical Center, Washington DC, USA

SESSION FIVE – CHAIR: Marvin Reid – DEBATE: BLOOD TRANSFUSION IS UNDER UTILIZED FOR SICKLE-RELATED COMPLICATIONS?

4:00pm **YES: Ross Fasano –** *Emory University School of Medicine, Washington, DC*

4:20pm **NO: Graham Serjeant –** *Sickle Cell Trust, Jamaica*

4:40pm **Debate**

5:00pm **DAY ONE CLOSE**

AGENDA Day Two: Friday October 11th 2019

8:30 am **Registration**

9:00 am **Welcome and Introduction**

SESSION ONE – CHAIR: Swee Lay Thein – TRANSLATION OF RESEARCH INTO CLINICAL CARE

9:10 am **CNS**
Fenella Kirkham
UCL Great Ormond Street Institute of Child Health, Southampton, Hampshire, UK

9:35 am **Respiratory Complications**
Parker Ruhl
National Institute of Allergies and Infectious Diseases, Bethesda, MD, USA

10:00 am **Cardiac Complications**
Vandana Sachdev (NHLBI, US)
National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, USA

10:25 am **Leg Ulcer**
Caterina P. Minniti
Albert Einstein College of Medicine, Bronx, NY, USA

10:50 am **Renal Complications**
Claire Sharpe (KCL, UK)
King's College London, London, UK

11:15 am **BREAK**

SESSION TWO – CHAIR: John Tisdale – OVERLOOKED BUT CRITICAL SPECIALTY AREAS IN SICKLE CELL DISEASE

11:35 am **Psychology in SCD**
Marsha Treadwell
Children's Hospital Oakland, Oakland, CA, USA

11:55 pm **Orthopedics and SCD**
Marcus Bankes (GSTT, London)
Guys and St Thomas' Foundation NHS Trust, London, UK

12:15 pm **Urology and SCD**
Belinda Morrison
Department of Surgery, Radiology, Anaesthesia and Intensive Care,
The University of the West Indies, Jamaica

12:35 pm **Pregnancy and SCD**
Monika Parshad-Asnani
The Caribbean Institute for Health Research, The Sickle Cell Unit,
The University of the West Indies, Jamaica

12:55 pm **LUNCH**

SESSION THREE – CHAIR: Georgianna Gordon-Strachan – PUBLIC HEALTH ASPECTS OF SICKLE CELL DISEASE MANAGEMENT

1:55 pm **Integration into PH in Developing Countries**
Jennifer Knight-Madden
The Caribbean Institute for Health Research, The Sickle Cell Unit, The University of the West Indies, Jamaica

2:20 pm **Insurance for Adults with SCD/Access**
Katherine Hassell (Denver, Colorado, US)
Colorado Sickle Cell Treatment and Research Center, University of Colorado, USA

2:40 pm **Education of Health Care Professionals – ECHO**
Rosalyn Stewart
Johns Hopkins Outpatient Center, Baltimore, USA

SESSION FOUR – CHAIR: Monika Asnani – DEBATE: PEOPLE WITH SCD SHOULD BE PRIMARILY CARED FOR BY HEMATOLOGISTS

3:00 pm **YES: Swee Lay Thein (NHLBI, US)**
National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, USA

3:20 pm **NO: Marvin Reid**
The Caribbean Institute for Health Research, The Tropical Metabolism Research Unit, The University of the West Indies, Jamaica

3:40 pm **Debate**

SESSION FIVE – PANEL DISCUSSION: CARE AND RESEARCH FROM THE PATIENT PERSPECTIVE

4:00 pm **Jamaica**
Morette Wright

4:20 pm **Trinidad & Tobago**
Renee Esdaille
Secretary of the Society for Inherited and Severe Blood Disorders T&T Ltd.

4:40 pm **United States**
Howard Woolley
President and CEO, *Howard Woolley Group*
Author, "Soar"

5:00 pm **Discussion**

5:20 pm **CLOSE OF CONFERENCE**

Monika Asnani, MBBS, DM, PhD
Senior Lecturer, *Caribbean Institute for Health Research*
Sickle Cell Unit
University of the West Indies, Mona Campus
Kingston, Jamaica

Monika Asnani is a Senior Lecturer at the Caribbean Institute for Health Research- Sickle Cell Unit, U.W.I. in Jamaica. She is a Family Physician and Epidemiologist with 16 years of providing clinical care for persons living with SCD. Her main focus of research has been (i) psychosocial outcomes and determinants in SCD especially during the adolescent years and (ii) sickle nephropathy. She is currently leading a project to assess the prevalence of neuropathic pain in SCD and is the local PI for the gene therapy in SCD project

She is the author of several papers in peer review journals and is an Academic Editor for Plos One journal. She has been awarded the Most Outstanding Researcher for 2015/16 & 2017/18 and Best Publication Award for Faculty of Medical Sciences of U.W.I. Mona for 2015/16. She is the Caribbean representative on the Worldwide Initiative on Social Studies in Hemoglobinopathies (WISSH) and a Board member of the Caribbean Researchers in Sickle Cell Disease & Thalassaemias (CAREST) group.

PREGNANCY & SCD

Due to advances in healthcare of persons with SCD, more girls and women are now entering the reproductive age group. There are many risks, both maternal and foetal, in a SCD pregnancy. The normal physiological changes that occur during a pregnancy can worsen the pathophysiologic processes that occur in SCD and will manifest especially in cardiac, respiratory and other haematological complications. There are many foetal complications that may occur such as prematurity, low birth weight and still births. An understanding of the effects of SCD on a pregnancy and the possibility of worsening of its complications such as pain events and infections, aggressive management in a high risk antenatal clinic and involvement of a multidisciplinary team in the care of the pregnant woman are all steps that can lead to positive outcomes.

Marcus J K Bankes BSc, FRCS (Orth)
Consultant Orthopedic Surgeon
Guy's & St Thomas' NHS Trust
London, UK

Marcus is the senior surgeon in the Hip Unit at Guy's and St Thomas' Foundation NHS Trust in London, UK, having been appointed Consultant Orthopaedic Surgeon in 2002.

His practice is exclusively confined to problems in and around the hip joint, with a special interest in surgical treatment of young adult hip disorders. He has nearly 20 years experience of total hip replacement surgery in sickle cell disease and has pioneered the use of modular stems with ceramic on ceramic bearings for this patient group.

He is a regular contributor at the British Hip Society, London Hip Meeting, and ISHA: The Hip Preservation Society as well as being a reviewer for a number of orthopaedic journals. He was one of the first users of the British Non-Arthroplasty Hip Registry was the first Chair of its Steering Group.
His interests outside work include film, TV and pop music, Apple electronic goods, North American Sport and cycling.

Orthopedics and Sickle Cell Disease
Vaso-occlusive episodes in SCD disrupt the blood supply to bone causing severe pain, and the potential to cause the death of segments of bone completely. This predisposes the bone to subsequent blood born infection (osteomyelitis OM) or avascular necrosis (AVN).

Avascular necrosis of the hips (AVN) is a very important treatable cause of pain and disability in patients with sickle cell disease. Involvement of larger segments of bone may compromise the structural integrity of the most important weight bearing part of the femoral head causing the bone to soften and collapse. If collapse occurs, there is irregularity of the joint surface, persisting pain and a high risk of secondary osteo-arthritis. If AVN is suspected plain xrays of the pelvis and a lateral view of the affected hip are obtained to demonstrate the presence or absence of collapse. If the xrays show that collapse has not occurred MRI is indicated to confirm the diagnosis and determine the extent of involvement of the femoral head. If collapse is visible no further imaging of this hip is required as the only effective surgical treatment is total hip replacement (THR), an operation which is able to transform the lives of disabled young men and women with SCD. Whilst traditionally the results of THR were poor in SCD, a number of developments have improved the outcomes dramatically in the last two decades now making THR a safe predictable operation. These include exchange transfusion, peri-operative antibiotics, uncemented implants, ceramic on ceramic bearing surfaces, and surgery performed in specialist centres with comprehensive SCD care. AVN is not the only cause of hip pain in SCD however and consideration should be given to other sources of pain such as the greater trochanter and lumbar spine, particularly as our sickle cell population ages.

Fernando F. Costa, M.D., Ph.D.
Professor of Hematology, *School of Medical Sciences*
State University of Campinas - UNICAMP
São Paulo, Brazil

Professor Fernando F. Costa graduated (1974) and obtained both his MSc (1979) and PhD (1981) degrees from the Ribeirão Preto School of Medicine of the University of São Paulo, where he also served as a faculty member (1985-1989). After completing a postdoctoral fellowship at the Yale School of Medicine (1987-1989), he joined the Department of Internal Medicine of the School of Medical Sciences of the University of Campinas (1990) and became a Full Professor of Hematology and Hemotherapy (1996).

Member of several national and international academic societies, Professor Costa has already published 425 papers in peer-reviewed journals and supervised 36 doctoral theses. He received a decoration from the Government of Brazil (2008) and has been awarded a great number of scientific prizes, including one from the Government of the State of São Paulo (2000).

At the University of Campinas, Professor Costa served as Dean of the School of Medical Sciences (1994-1998), Director of the Hematology and Hemotherapy Center (1998-2002), Vice-President for Research (2002-2005) and General Coordinator of the University (2005-2009). He was the president of the University of Campinas from April 2009 to April 2013. He was a member of the Superior Council of the São Paulo Research Foundation (FAPESP) from 2012 to 2018 and, since 2013, he has been Editor-in-chief of the Brazilian Journal of Hematology and Hemotherapy.

SICKLE CELL DISEASE AROUND THE WORLD- BRAZIL

Brazil is the largest country in South America with an estimated population of 208 million inhabitants in 2018. The population presents a very heterogeneous ethnic origin and its distribution is also diverse in different regions of the country. The available data estimate that there are 30,000 to 50,000 patients with sickle cell disease (SCD) in the entire country. The prevalence of the β^s allele ranges from 1.2% to 10.8%, according to the region of the country, while the prevalence of the β^c allele is estimated to be between 0.15% and 7.4%.

There has been a well structured and well funded newborn screening program in Brazil since 2001 (National Neonatal Screening Program), which is available in all 26 states of the country although the coverage is heterogeneous among different regions. As a consequence of the program, some studies concerning the survival of children with SCD in Brazil have been published. Although the number of deaths in the country is still high, compared to Europe, the data suggest an improvement in the care of patients and in their survival. The Bantu haplotype is predominant among sickle cell anemia (SCA) patients in Brazil, with the exception of the state of Bahia, where there is a high proportion of Benin Haplotype. Patients from Brazil, at a genetic level, show more admixture and a high European background, compared to patients in the United States. Special centers for the diagnosis and treatment of SCD with the support of the Ministry of Health by the Public Healthcare System (called SUS) were developed in almost all states of Brazil to provide clinical care for patients. In addition to free medical care, they provide blood transfusion, penicillin prophylaxis, immunization, hydroxyurea and other drugs to the patients. Several studies concerning a number of aspects of SCD have been carried out in these centers, for example, genomic polymorphisms and possible implications for clinical diversity, aspects of pregnancy in SCD, priapism, vaso-occlusion, inflammation, transfusion and alloimmunization. In fact, several important clinical aspects of SCD have been reported in Brazil concerning leg ulcers, pulmonary hypertension, abnormalities of conjunctive and retinal vessels, cognitive profiles of children with SCD, hypercoagulability markers in HbSC disease and bone marrow transplantation. Some studies have indicated that the survival of patients with SCD in Brazil is 21.3 years less than the life expectancy of the general Brazilian population and that the most frequent causes of death are acute chest syndrome, infection, stroke, chronic organ damage and death during “acute crisis”. An important fact for the future of clinical care of patients with SCD in Brazil is to increase or, at least, to maintain constant the budget for the Brazilian national health system, the SUS.

Susanna Curtis, M.D., Ph.D. Candidate
Post-Doctoral Fellow, *Hematology Department*
Yale Cancer Center
New Haven, CT, USA

Dr. Susanna Curtis is a post-doctoral fellow in hematology at the Yale Cancer Center and a PhD candidate in Investigative Medicine in the Yale Graduate School of Arts and Sciences.

Dr. Curtis completed medical school at New York Medical College and fellowship in Internal Medicine at Montefiore Medical Center where she developed an interest in sickle cell disease research. She completed her fellowship in hematology and oncology at Yale University where she received the Annual Fellow's Award for Outstanding Research in Hematology. Her previous research identified serum markers of morbidity and mortality in sickle cell disease. Her PhD thesis focuses on the effects of cannabinoids on pain and inflammation in sickle cell disease.

OPIOID AND MARIJUANA IN SCD

Cannabinoid use is common among patients with sickle cell disease, but little is known about the risks or benefits of cannabinoids in this population. This talk will review: effects of cannabinoids on opioid use in other diseases of pain, cannabinoids in murine models of sickle cell disease, patterns of cannabinoid and opioid use among adults with sickle cell disease, and ongoing studies of cannabinoids in patients with sickle cell disease.

Deepika Darbari, M.B.B.S., M.S.
Attending Physician, *Division of Hematology, Children's National Medical Center*
Associate Professor of Pediatrics, *George Washington University School of Medicine and Health Sciences, Washington, DC, USA*

Dr. Darbari is a Pediatric Hematologist-Oncologist at the Children's National Medical Center and Associate Professor of Pediatrics at the George Washington University in Washington DC. Dr. Darbari studies complications of sickle cell disease with emphasis on pain. She has been conducting clinical and translational studies directed towards a better understanding of mechanisms of sickle cell pain and its management using pharmacologic and non-pharmacologic modalities such as acupuncture. Her research has contributed to understanding variability of pain experience in patients with sickle cell disease. Her team had described presence of altered brain connectivity in patients with sickle cell disease who needed frequent hospitalization for pain. More recently her work has shown some of the risk factors for persistence of pain and opioid use after being cured of sickle cell disease by hematopoietic bone marrow transplant. She has published many peer reviewed papers on the subject. She has contributed to the development of diagnostic criteria for acute and chronic pain in sickle cell disease. She has served as the chair of the non-patient reported outcomes of pain at the recent FDA/ American Society of Hematology (ASH) sickle cell disease endpoint workshop and has also represented ASH for amendment of CDC guidelines on opioid use in sickle cell disease.

PAIN AS A COMPLEX PHENOTYPE

Pain is the most common symptom experienced by patients with sickle cell disease (SCD) which contributes to poor quality of life, increased morbidity and high health care cost. High burden of pain is also associated with shortened life span. Patients with SCD may exhibit diverse pain phenotypes resulting from different underlying mechanisms. Episodes of acute pain, commonly known as painful vaso-occlusive episodes or crises are the hallmark of SCD; however chronic pain is also common especially in adults with SCD. Furthermore, patients may also experience a mixed phenotype of acute pain on the background of chronic pain. Acute SCD pain is considered to be due to ischemia-reperfusion injury and inflammation resulting from vaso-occlusion while chronic pain likely results from mechanisms such as peripheral and central sensitization which leads to altered pain processing. Chronic pain can also be caused by SCD related complications such as avascular necrosis of hip and leg ulcers. It is important to recognize that any of these underlying mechanisms of pain may be operative simultaneously in a patient. Evidence suggests that phenotypes of pain can impact the responsiveness to different therapies. Recently described diagnostic criteria for acute and chronic SCD pain developed in collaboration with American Pain Society are helpful in determining pain phenotypes and may help with individualization of pain management in patients with SCD.

Jacques Elion, M.D., Ph.D.
Professor
Université de Paris, Insem 1134, Institut National de la Transfusion Sanguine, Paris, France

Dr Elion received his MD from Paris Descartes and a PhD from Paris Diderot Universities. He was a Research Assistant at the Mayo Graduate School of Medicine, University of Minnesota and a Fogarty Scientist at the US National Institutes of Health. Dr Elion is Professor of Molecular Genetics at the Université de Paris and Visiting Professor at the Universidade de São Paulo. He is the former Director of the Dept of Medical Genetics at the Robert Debré University Hospital. Dr Elion's research is focused on pathophysiology, prevention and global care of SCD. It is conducted at Unit 1134 of the French National Institute of Health and Medical Research (Inserm) sheltered by the National Institute of Blood Transfusion in Paris and at the University Hospital in Guadeloupe. The Unit is part of the French Laboratory of Excellence on the Red Cell (GR-Ex). Dr Elion has developed extensive international collaborations notably in sub-Saharan Africa, India, the Caribbean and Brazil. Dr Elion has organized and chaired several international meetings, including the scientific session at the inaugural ceremony for the 1stWorld SCD Day, June 19, 2009, UN Headquarters, NYC.

SICKLE CELL DISEASE AROUND THE WORLD- EUROPE

Europe is composed of 50 sovereign states. Among them 28 are part of the European Union (EU), the population of which reaches 513 million. In addition to its continental countries, EU extends to 8 outermost regions, including the Caribbean islands of Guadeloupe and Martinique, and French Guiana where populations of African descent predominate, as well as the islands of La Reunion and Mayotte in the Indian Ocean.

In continental EU, sickle cell disease (SCD) is both endogenous in the Southern countries (Greece, Southern Italy, Portugal) and the result of past migrations from sub-Saharan Africa, the Caribbean and the Indian sub-continent. But migration patterns from the Middle East and Africa have changed dramatically over the past decade. Between 2010 and 2017, nearly 1 million sub-Saharan African migrants have sought asylum in Europe, and that trend is projected to continue into the future. This, of course, is important when considering the very high prevalence of sickle cell trait and disease in these parts of the world. This has created a high contrast in countries with a past history of migrations (like France and the UK) in which sophisticated systems of care and prevention have been developed and countries with low incidence rates now facing a recent and rapidly changing migrant flow where patients are often under-diagnosed and follow-up paths insufficiently defined.

Although the history of newborn screening (NBS) for SCD in Europe goes back almost 40 years, the situation is highly heterogenous from one country to another. France and the UK were the first to introduce SCD screening in the 1980's and to extend its coverage to their entire national territories in the 2000's. The Netherlands, Spain and Malta now have also national programs. Belgium screens in the regions of Brussels and Liège, Ireland has been running a pilot for many years. Italy and Germany have completed several pilot studies but are still in the preparatory phase of national NBS programs for SCD. In continental France a "targeted"approach is used in which testing is restricted to babies whose parental family origins are from 'at risk' ethnic groups. In contrast,for all the other programs and in the French overseas regions, a "universal screening" is offered to all newborns, irrespective of family origins.

At this stage, precise incidence data are available only for the UK and France with rather similar situations in the two countries (300-400 affected newborns yearly in each country; incidence 1/2000-1/1800). In both countries, the incidence rate is highly heterogeneous from one region to another with highest values in megapolises: London, Manchester, Birmingham in the UK and Paris in France (incidence 1/824). In France, the incidence of affected newborns has increased by 24% from 2006 to 2016. The exact total number of patients in each country is unknown as the patient's registry in the UK is too recent and only being initiated in France.

In the UK and France, rather comparable sophisticated comprehensive programs of care have been developed that are free of charge for the patients. The French program is part of the National Program for Rare Diseases. It is characterized by a dense network of reference and competence centers, a strong connection with the general practitioners and the patient's associations, and also with clinical and basic research in particular with the Laboratory of Excellence on the Red Cell (GR-Ex). The EU has recently launched an initiative for the implementation of European Reference Networks (ERNs). EuroBloodNet is at work to coordinate and uniformize comprehensive care for hematological diseases including SCD in Europe.

Lobitz, S., Telfer P., et al. *Br J Haematol*. 2018; 183:648-66

Daniel Y., Elion J., et al. I*nt. J. Neonatal Screen*. 2019;5: 8-12

Ross Fasano, M.D.
Associate Professor, *Departments of Laboratory Medicine, Hematology, Emory School of Medicine*
Director of Apheresis, Associate Director of Transfusion & Tissue Services, *Children's Healthcare of Atlanta, Atlanta, Georgia, USA*

Dr. Ross Fasano is an Associate Professor of Pathology and Laboratory Medicine and Pediatric Hematology/Oncology at Emory University School of Medicine. He also has an adjunct appointment in Adult Hematology and provides comprehensive care to adult patients with sickle cell disease at Grady Memorial Hospital. His clinical expertise is in pediatric transfusion and hematology, with an emphasis on chronic transfusion therapy for children and adults with sickle cell disease. He is one of the few physicians in the country trained in Pediatrics, Pediatric Hematology/Oncology, and Blood Banking/Transfusion Medicine. He is the associate director of the blood banks at Children's Healthcare of Atlanta, and Director of Apheresis at Children's Healthcare of Atlanta. His research focuses on clinical outcomes and complications of RBC transfusion, specifically alloimmunization and iron overload in patients with hemoglobinopathies. During his training and subsequent practice of medicine, he has had extensive clinical experience in managing heavily alloimmunized and iron overloaded patients with sickle cell disease.

BLOOD TRANSFUSION IS UNDER UTILIZED FOR SICKLE-RELATED COMPLICATIONS- YES

Red blood cell (RBC) transfusion therapy is a key component of the comprehensive management of patients with sickle cell disease (SCD), and has dramatically changed the natural history of stroke (re) occurrence in children. Additionally, RBC transfusions have been proven to be lifesaving for many acute sickle cell-related complications. Although episodic and chronic transfusions have significantly improved the morbidity and mortality of patients with SCD, transfusions are underutilized in many clinical settings. Using chronic transfusion therapy for primary and secondary stroke prevention as a paradigm, this discussion will provide evidence on how RBC transfusion therapy should be expanded upon for many different aspects of SCD management.

Marie-Dominique Hardy-Dessources, Ph.D.
Senior Research Officer, *INSERM Institute*
French National Institute for Health and Medical Research
Universite des Antilles, Pointe a Pitre, Guadaloupe

Dr. Marie-Dominique HARDY-DESSOURCES is a biochemist educated at the University Paris XI, Orsay, France. She obtained her PhD from the pharmaceutical department of this University. She conducted her first research studies at the Research Unit 91 of the French National Institute of Health and Medical Research (Inserm), at Henri Mondor Hospital Creteil, France. These studies, focused on hemoglobin S polymerization and attempts to prevent its polymerization, are published under her married name: Marie-Dominique RHODA.

In 1987, she was hired by Inserm as a researcher and joined a small team in Guadeloupe (French West Indies) attached to the Unit 91 Inserm and directed by Guy MERAULT. She was involved, alongside Guy MERAULT, in the creation of the Sickle Cell Center of Guadeloupe directed today by Dr. Maryse Etienne-Julan.

She's currently pursuing her research in the Guadeloupean group attached to the Inserm Unit 1134 based both in mainland France and Guadeloupe and directed by Yves Colin-Aronovicz.

Her research projects are conducted in the framework of basic and translational research and include two main axes: 1) study of the mechanisms of activation of the red blood cell leading to vasoocclusive crises; 2) the relationships between the severity of sickle cell disease, blood rheological properties, cellular inflammation and oxidation.

She is the President of the Caribbean network of research on sickle cell disease and thalassemia (CAREST), since its official structuring in 2012 as a non-profit organization under French law.

SICKLE CELL DISEASE AROUND THE WORLD- THE CARIBBEAN

Defining the Caribbean region is challenging since the delimitations of its borders depend on the criteria used. The Geopolitical criteria bring the concept of the great Caribbean defined as a large area including the Caribbean Sea, more than 700 islands,the Caribbean facade of Central America and the coastal plains of Colombia, Venezuela and Guyana. It is above all, a region marked by a particular history, that of slavery and sugar cane plantations. From the sixteenth century to the nineteenth century, more than 12 million forcefully enslaved Africans and half a million Asian indentured laborers migrated to this region. The sickle cell gene, with a predominant African or Asian origin according to the settlement of the Caribbean populations, appears as a common feature between these peoples.

Estimated data suggest a high prevalence of sickle cell disease (SCD) in the Caribbean; however, prior to 2006, few accurate SCD prevalence and epidemiological data were available. These data were provided from newborn screening (NBS) programs implemented in Jamaica andin the French territories and from a prenatal diagnosis program in Cuba; all these islands, unlike other Caribbean regions, have specialized centres for providing comprehensive clinical care facility for the management of SCD. Nowadays, beyond universal NBS programs performed in this first group of islands, pilot NBS programs have been performed in several other Caribbean countries, providing a larger view of SCD prevalence in the Caribbean (1-3). However, screening is most often interrupted when the pilot project ends since governments are unwilling to support the continuation of these programs because of their high cost.The evolution towards the use of rapid tests, less expensive, is an alternative which is currently under evaluation in different Caribbean regions. The Caribbean Network of Researchers on Sickle Cell Disease and Thalassemia (CAREST) formally founded in 2011 and other regional stakeholders with common goals, including the SickKids-Caribbean Initiative, participate fully in the extension and sustainability of these NBS programs, urgently needed to improve the clinical management of SCD patients in the Caribbean area.

Clinical Care Guidelines provided by the French Health Authority or by the Jamaican Sickle Cell Unit are currently used in the Caribbean region. Once SCD infants are identified, referral for care is set up. However, the shipment of blood specimen to the central laboratories located in Guadeloupe and Jamaica where the screening is performed causes, in some cases, a significant delay before the results are obtained and transmitted, compromising delivery of early medical care.

In absence of NBS, patients are most often diagnosed when they are admitted in the hospital for a complication. Medical healthcare is usually given by paediatricians or by haematologists. Usually, to overcome the lack of well-balanced healthcare organizations, health professionals rely on patients' associations.

Hydroxyurea appears as the most widely therapeutic option used in the region, while other potential therapeutic options such as chronic blood transfusions or stem cell transplantation are more accessible to the French overseas territories.

Scientists from Jamaica, Cuba and Guadeloupe, in the framework of CAREST network, have successfully completed research projects to explore SCD markers severity and promotion of bilateral exchange training opportunities for young scientists (4). Working groups are being set up to ensure the continuation of research programmes and the extension of neonatal screening in this region.

CAREST also organizes regular conferences to spearhead the advances in terms of clinical management and research and facilitate the development of larger collaborations. Indeed, CAREST's presence, which was limited to Caribbean islands, has now been extended to the Greater Caribbean since the fifth conference of CAREST which took place in French Guiana in October 2018, strengthening interactions between the insular Caribbean and other countries such as Costa Rica, Nicaragua, Colombia and Venezuela.

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Kathryn Hassell, M.D.
Professor of Medicine, *Division of Hematology*
Director, *Colorado Sickle Cell Treatment and Research Center*
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Dr. Kathryn Hassell is a Professor of Medicine and Director of the Colorado Sickle Cell Center and inpatient and outpatient pharmacy-directed anticoagulation services at the University of Colorado Denver. She completed her Bachelor's of Art in Medical Technology at the College of St. Scholastica and her medical

education at University School Minnesota School of Medicine, internal medicine residency at the University of North Carolina-Chapel Hill and fellowship in Hematology/Oncology at the University of Colorado Denver. Her interest and expertise includes academic specialty practice, clinical and translational research in hemoglobinopathies, thrombotic disorders and anticoagulation. Dr. Hassell is an active member of the American Society of Hematology, International Society of Thrombosis and Hemostasis, and the American Pain Society. She co-chairs and serves on a number of national steering committees for multicenter clinical trials and federal projects sponsored by NIH, HRSA and CDC, and is the founder of the Sickle Cell Adult Provider Network, an organization which seeks to enhance research collaboration and communication across the adult sickle cell provider community. She has published numerous articles and other work in her field and participated in guideline and registry development. Dr. Hassell lectures nationally and internationally on sickle cell disease, thrombotic disorders and anticoagulation. In her spare time, she enjoys the mountains of Colorado and medical missionary work in Central America and Africa.

SICKLE CELL DISEASE AROUND THE WORLD- UNITES STATES OF AMERICA

Sickle cell disease affects an estimated 100,000 – 120,000 individuals with sickle cell disease in the United States, of which at least 50% are adults. The majority of these persons live in urban or suburban areas, although a segment of the population lives in rural areas, distant from larger healthcare facilities with specialty services. Since sickle cell disease is a rare disorder in the US population, the majority of healthcare providers and systems are unfamiliar with its manifestations and management. This is particularly problematic for individuals who are not within a catchment area of established sickle cell centers. This is further complicated by the reliance on the public health insurance programs Medicaid and Medicare, as well as national concerns about the "opioid crisis", factors which may limit access to quality healthcare. There are a number of guidelines for the management of sickle cell disease, including those released by the National Heart, Lung and Blood Institute (NHLBI) in 2014 targeting primary care providers, and the anticipated release of specialty care guidelines from the American Society of Hematology (ASH) in late 2019 and 2020. Policy statements from the Center for Disease Control and Prevention (CDC) and the Center for Medicare and Medicaid Services (CMS) emphasize the need to exclude sickle cell disease from restrictions on opioid use, noting pain in this disease should be managed as for patients with cancer and other severely painful disorders. However, there has been limited implementation of these guidelines and recommendations across the healthcare system, particularly outside of specialized sickle cell centers. This problem has been targeted by the NHLBI's Sickle Cell Disease Implementation Consortium and by the Health Resources and Services Administration (HRSA) through its Sickle Cell Services Demonstration Program. A major Patient-Centered Outcomes Research Institute (PCORI) program funds comparative effectiveness research for transfer of care from pediatric to adult healthcare. Growing interest, including from the biotechnology/pharmaceutical industry, has resulted in over 140 active clinical research studies recruiting subjects in the US. These range from translational, Phase I-VI interventional trials to investigation of psychosocial aspects as use of technologies. The NHLBI's Cure Sickle Cell Initiative seeks to accelerate the development of gene therapy. Efforts to improve coordination between these multiple activities are ongoing, through the Health and Human Services (HHS) Sickle Cell Disease Working Group and ASH's

Sickle Cell Disease Coalition and organization of a clinical trials network. At the request of HHS, the National Academy of Sciences has convened an *ad hoc* committee to develop a strategic plan and national blueprint for action, an important activity given some duplication of and competition between efforts. Overall, there has been growing awareness of and increasing attention to those living with sickle cell disease in the US.

INSURANCE FOR ADULTS WITH SCD/ACCESS

Individuals with sickle cell disease require access to healthcare systems, medical practitioners and other service providers that can address this complex multi-system condition which affects all aspects of health and life, with major physical, psychological and socioeconomic impact across the lifespan. Multiple factors play a role in whether or not an individual is receiving the care necessary to optimize their health.

An essential component of optimal care is the existence of a healthcare system that has the necessary diagnostic and therapeutic capacity to manage sickle cell disease. Even if the proper testing and treatment modalities are in place, these are most effectively utilized by providers who are knowledgeable about sickle cell disease. In many places around the world, and even in the most developed countries with sophisticated healthcare systems, local healthcare facilities may lack these facilities, technologies, therapeutic options and/or informed providers. Thus, while these systems may be accessed, optimal care is not achieved.

Even when appropriate systems exist, they may not be accessible because of distance or because the cost of care is prohibitive. In some countries this occurs when national ("universal") healthcare programs do not have the resources to provide certain aspects of care and parallel "private pay" systems are too expensive. In the United States, access to healthcare hinges on an individual's ability to obtain health insurance, either through public programs or often through employment-based private insurance coverage. Those who have insurance coverage may not have plans that permit attendance at facilities where there is the capacity to care for sickle cell disease, or are "under-insured" by plans that do not pay for recommended testing and therapies. This is also challenging for those who are employed, making them ineligible for public programs, but are un- or underinsured through their workplace. Thus, while appropriate healthcare is available, it may not be accessible to individuals due to lack of coverage for services and inability to pay out of pocket.

Another important element for delivery of optimal care, which is often overlooked, is engagement of healthcare by individuals and their families. Competing basic priorities including food, housing and maintaining employment force choices about accessing healthcare and adherence to disease management. Cultural and psychosocial factors impact these decisions. In addition, adolescents and young adults may elect to "opt out" of healthcare during this particularly challenging developmental period even when there are no barriers to optimal healthcare.

Given the many different aspects potentially affecting utilization of optimal healthcare, a careful analysis of strengths and gaps is warranted to guide development of targeted solutions for those living with sickle cell disease.

Matthew Heeney, M.D.
Clinical Director, *Pediatric Blood Disorders Center*
Associate Chief, *Hematology*
Director, *Sickle Cell Program*
Assistant Professor in Pediatrics, *Harvard Medical School, Boston, MA, USA*

Dr. Matthew Heeney received his MD at the University of Calgary, Alberta, completed his residency at the Montreal Children's Hospital, McGill University, and a pediatric Hematology/Oncology fellowship at Duke University. In 2002 he joined the staff at Boston Children's Hospital and Harvard Medical School as the Pediatric Hematology Clinic Directorat Boston Children's Hospital (BCH) and Assistant Professor of Pediatrics at Harvard Medical School. Dr. Heeney is now the Associate Chief of Hematology and Director of the Sickle Cell Program at Boston Children's and also the Director of the Blood Disorders Center at Dana-Farber/Boston Children's Cancer and Blood Disorders Center.

Dr. Heeney is a clinical investigator in sickle cell disease. He has been Boston Children's principal investigator or site investigator for many NIH-funded clinical trial consortia and both NIH- and Industry-funded multicenter clinical trials in sickle cell disease. Dr. Heeney also conducts translational research in inherited disorders of iron homeostasis in humans. In particular he is interested in investigating the genetic basis inherited disorders of iron deficiency, sideroblastic anemia and iron overload.

Dr. Heeney is also an active educator. For the past decade he has co-lead the Hematology Course for the Harvard Medical School undergraduate curriculum. He is also a lecturer for many CME courses including Board Review courses for American Society of Pediatric Hematology/Oncology (ASPH/O), Harvard Medical School (HMS), Dana-Farber Cancer Institute, Baylor College of Medicine, Scripps Institute, and Brigham & Women's Hospital.

UPDATE ON CLINICAL TRIALS

Dr. Heeney will review the recent and current clinical trials of pathophysiologically-directed medical therapies for sickle cell disease. This will include manipulation of hemoglobin oxygen dissociation, selectin inhibition, platelet inhibition, and manipulation of the Nitric Oxide/cGMP pathway.

Matthew Hsieh, M.D.
Staff Clinician, *Cellular and Molecular Therapeutics Branch*
National Heart, Lung, and Blood Institute
National Institutes of Health, Bethesda, MD, USA

The success of an earlier murine model in our group led to our first clinical trial of hematopoietic cell transplantation (HCT) in sickle cell disease (SCD), testing a non-myeloablative regimen of 300 rads of total body irradiation, alemtuzumab and sirolimus to further reduce the risk of GvHD, with fully matched related donors. I have focused my clinical effort over the last decade in running this clinical trial (NCT00061568). After expanded enrollment, the regimen remains minimally toxic and is applicable to patients with severe

organ damage. Overall survival remains at 90% with no acute or chronic GvHD. These highly desirable outcomes led to this regimen being the backbone of a modified matched related donor study for those at higher risk of graft failure (NCT002105766), as well as our haplo-identical transplant regimens (NCT00977691, NCT03077542). Our rationale of using lower intensity conditioning regimen to minimize the tissue injury from radiation and/or chemotherapy, modulating lymphocytes to promote graft tolerance, and achieving stable mixed chimerism post-transplant without GvHD, have generated enthusiasm among the transplant community to expand this treatment to adult and pediatric patients with SCD. Several transplant centers have replicated this non-ablative approach with equally positive results. Patients and advocacy groups have an increased awareness about allogeneic HCT and are routinely asking their medical providers to see if transplant is an option in their overall SCD care.

LONG TERM OUTCOMES OF BMT

Allogeneic HCT have been increasingly utilized as a curative option in SCD. Myeloablative and non-myeloablative regimens using matched related donor (MRD) HCT have demonstrated high efficacy and are well tolerated. As results from recent haploidentical HCT have improved dramatically, this donor source is increasingly recognized as a viable alternative among patients with severe disease but without MRD. Benefits of successful HCT include improvements in hemoglobin, resolution of hemolysis, and quality of life measures. Long term and late complications of HCT are infrequent, and could include changes in the thyroid, heart, lung, and renal function. Secondary cancers in the marrow and solid organs have been rarely reported, thus screening remains important in post-transplant care. Recently, reduction in transcranial Doppler cerebral velocities in children with abnormal TCD was shown at 1 and 3 years post-transplant, compared to continuation of chronic exchange transfusion. In our cohort of young and older adults who underwent MRD HCT, thyroid disorder occurred in 10%; heart function, with respect to ejection fraction, was preserved in the majority of patients. There was also an improvement in the anemia associated dilated cardiomyopathy. Lung function post HCT was overall stable: forced expiratory volume (FEV1) was stable in most while 20% had about 10% decrease. The diffusing capacity for carbon monoxide (DLCO) was stable to increased in most, while 15% of the patients also had about 10% decrease, possibly due to weight gain. 6 minute walk test were increased in 40% and stable in 50% of the patients.

Dipty Jain, M.D.
Professor and Head, *Department of Pediatrics*
Government Medical College
Nagpur, India

Dr. Dipty Lalit Jain is the current Professor and Head, Department of Pediatrics, Govt. Medical College, Nagpur and she is a consultant for WHO (UIP), USAID (Domestic Violence Against Women and Children Scientific Advisory Committee member, Indian Council Medical Research (ICMR). She has 45 years of teaching experience and was awarded the 'Best Teacher Award' in the year 2011. She completed her undergraduate and postgraduate schooling from Nagpur University and M.Sc (Clinical Epidemiology) from Mc. Master University, Canada.

She is very active in the field of research and has been awarded the best paper award for "Hydroxurea in SCD" at the second International Meet on Sickle Cell Disease, "Natural History of Sickle Cell Disease" at National Pediatric Hematology and also for the paper 'Fixed Low Dose Hydroxurea in Children with Sickle Cell Disease'. Her pro-activeness for research also translates into the multiple international and national Publications she has been credited.

She has been awarded the 'Rockfellor Fellowship' for the year 1991-92. MSc Master University, Canada for Masters in Med (Clinical Epidemiology) with a special course on Health Economics, and also is a Member of International Clinical Epidemiology Network (INCLEN) Philadelphia, PA.

Apart from the astounding academical achievements, her contribution towards society in the middle-income countries like India is astonishing. Her case control study, "Physical Abuse During Pregnancy and Low Birth Weight Infant" was awarded the best paper award at a conference held at Trivendram, India. She is also the President of INSPACAN-Indian Society for the Prevention of Child Abuse and Neglect, affiliated by ISPCAN-International Society for the Prevention of Child Abuse and Neglect.

Her innovative and unique work in the field of Sickle Cell Disease is unparalleled to anyone in the country and she is a member of the Global Sickle Cell Disease Network (GSCDN) International Advisory Council, ICMR and Government of India Policy on Sickle Disease is determined by her and has trained faculty of Medical and Paramedical on Sickle Cell Disease in the entire country, also she is the reviewer for Clinical Evidence on Sickle Cell Disease in British Medical Journal (BMJ).

What she gives back to the society is what defines her. She has aptly been awarded "Woman of the year in 2002-2003 by the United States of America"

SICKLE CELL DISEASE AROUND THE WORLD- INDIA

India is a vast country with hugely diverse genetic pool of individuals. Hemoglobinopathies are found all over India with certain ethnic groups or communities having greater share of disease burden and carrier state. Despite increased urbanization, greater access to education especially within women, government policies and various intervention measures the hemoglobinopathies especially Sickle Cell disorders have witnessed a consistent increase in disease numbers. This could be because of better and handy diagnostic methodologies, clinician awareness and vigilance. The aim of this presentation is to share the diverse disease patterns which exist within different geographical regions and communities hailing from various socio-economic strata. The disease complications and their management pose significant challenge and strain on resource limited healthcare system which is predominantly pubic funded and remains underinvested to be able to serve vast population of patients. Several screening, early diagnosis and holistic care models have been tried at various centers in geographical areas where Sickle cell disease is endemic.

In the era of gene editing one of global epicenter of sickle cell disease - India witnesses poor access and compliance to gold standard treatment hydroxyurea and debilitating complication stroke limiting measures like TCD (Trans Cranial Doppler). Government Medical College Nagpur located in central India is a

public funded teaching hospital which has been pioneer in setting new standards of care for patients suffering from various hemoglobinopathies especially Sickle Cell Disease. Specialised Sickle care clinic operated at the department of pediatrics is also represented by different clinical specialties like Surgery, Orthopedics, OBG, Ophthalmology, Hematology, Radiology, Psychiatry along with experienced counsellors. This clinic provides comprehensive care and also counsels the patients for the need of pre-marital, perinatal and neonatal screening. Under one roof the patients get complete care and they do not have to run from pillar to post for getting appropriate treatment for various complications. Most often the patients hail from poor socio-economic strata and patient care providers are daily wage earners. This single roof care model saves time and ensures greater patient compliance. Perhaps this model could be replicated across all resource poor countries which may result in limiting complications, improve patient outcomes and most important create productive citizens who contribute positively to the society rather being an economic burden.

Fenella Kirkham

Consultant Pediatric Neurologist, *University Hospital, Southampton and King's College Hospital*

Professor, *Pediatric Neurology, Developmental Neurosciences and Biomedical Science Units, UCL Great Ormond Street Institute of Child Health and Clinical and Experimental Sciences, University of Southampton*

Fenella Kirkham is a paediatric neurologist with an interest in prevention and treatment of disabling acute and chronic paediatric neurological problems, specifically in the context of sickle cell anaemia. She has developed an interest in the role of sleep in cognition in sickle cell disease and is currently analysing data from the East London and Sleep Asthma cohorts with her Post-docs, PhD and MSc students. She collaborates with haematologists in England, Europe, the USA and Africa. She ran a Phase II randomised controlled trial of auto-adjusting continuous positive airways pressure with cognitive and magnetic resonance imaging (MRI) endpoints in children and adults. She has funding for a randomised controlled trial of Montelukast in children aged 3-8 years with the primary endpoint being the NIH toolbox processing speed.

CNS

Jennifer Knight-Madden M.B., B.S., Ph.D.

Professor, *Pediatric Pulmonology & Clinical Research*

Director, *Sickle Cell Unit*

Caribbean Institute for Health Research, University of West Indies

Kingston, Jamaica

Dr. Jennifer Knight-Madden completed medical school at the University of the West Indies, Jamaica. Her postgraduate training included a residency in Pediatrics at the Hospital for Sick Children (SickKids), Toronto and a Pediatric Pulmonology Fellowship and MSc in Biometry at Duke University Medical School. She completed her PhD at Kings College, London which examined the role of asthma in the pulmonary complication of sickle cell disease (SCD). Her main research interests are the pulmonary complications of

sickle cell disease, asthma, newborn screening for SCD and implementation science. She is the author of two book chapters and several articles in peer reviewed journals. She has been on faculty at the Sickle Cell Unit, Caribbean Institute for Health Research, the University of the West Indies since 1997 and was appointed as Director in 2013.

INTEGRATION INTO PUBLIC HEALTH IN DEVELOPING COUNTRIES

There is no discounting the massive importance of research to the improvement of care for persons living with sickle cell disease. However, for this knowledge to have full impact, it must be integrated into public health services. The tenets of public health include the importance of maintaining health, preventing or attenuating the effects of disease and concepts such as access, equity and quality. While it is not possible to have a "champagne health system on a pepsi budget" in developing countries, the integration of promotion, prevention, treatment, cure and rehabilitation for people living with sickle cell disease (SCD) into the public health system, utilizing primary health care as well as specialist services, can improve the care received by patients and, may well decrease the cost to the system. A case study of the process in Jamaica, with lessons learned regionally, gives insight into the facilitators and barriers to the implementation of a truly integrated program for SCD within the public health system.

Prof. Julie Makani
Head, *Department of Hematology and Blood Transfusion*
Muhimbili University of Health and Allied Sciences (MUHAS)
Dar es Salaam, Tanzania

My area of interest is haematology as a clinical area, with a focus on sickle cell disease (SCD), which requires a multi-disciplinary approach, skills, knowledge, and network connections.

I am based at Muhimbili University of Health and Allied Sciences (MUHAS) http://www.muhas.ac.tz, which is the main clinical http://www.mnh.or.tz/, academic and research centre in Tanzania. MUHAS has established a systematic framework for comprehensive SCD research at Muhimbili National Hospital (MNH). With prospective surveillance of over 5,000 SCD patients; this is one of the largest single-center research programs in the world. Funding has been from the Wellcome Trust [2003 – 2017] and more recently from National Institutes of Health (2015 – 2022) being a principal investigator (PI) on the Sickle Pan African Research Consortium (SPARCO) in Tanzania, Ghana and Nigeria http://www.sickleinafrica.org/. I also serve as co-PI on SickleGenAfrica, investigating the genetic basis of disease progression http://sicklegenafrica.com/ The Sickle Cell Programme also receives support from other sources of funding in health, research and education as it is integrated into providing healthcare, working to influence health policy and introducing programs for SCD in Tanzania. I have been involved in establishing networks at institutional, national, regional (**REDAC**); African (Sickle Pan-African Network - 17 countries), and global level (http://www.globalsicklecelldisease.org). In order to develop a platform for advocacy, I was involved in setting up the Sickle Cell Foundation of Tanzania (2010) and I am a member of the Tanzania Sickle Cell Disease Alliance (2016).

As part of academic and scientific development, we have developed educational programs in biomedical and clinical sciences at undergraduate and postgraduate level, at MUHAS. I have developed experience and expertise in cross-cutting skills and knowledge which allow me to significantly contribute to professional development of clinicians and scientists who are working to establish independent careers. The areas include clinical epidemiology and research methods including study design, patient registry development, data collection, management and analysis. In addition, I am able to provide guidance in grant application and grant management as well as building networks in research, healthcare and education. Muhimbili partners include the American Society of Hematology global programme (http://stage.hematology.org/Global/204.aspx, University of California Global Health Institute (UCGHI) GloCal Health Fellowship http://www.glocalfellows.org/international/Pages/Tanzania.aspx. I was involved in developing the white paper for the Human Hereditary for Health in Africa (H3Africa) initiative as well as a commissioner of the NCD lancet commissioner for Poverty. The aim is to build a critical mass of individuals with expertise in health and biomedical sciences who are able to develop their respective fields in Tanzania and Africa whilst developing global partnerships.

SICKLE CELL DISEASE AROUND THE WORLD- AFRICA

Punam Malik, M.D., M.S., M.B.B.S.
Director, *Cincinnati Comprehensive Sickle Cell Center*
Director, *Translational Core Laboratory*
Professor, *UC Department of Pediatrics*
Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

Dr. Malik is a physician-scientist, who has worked on hematological disorders for the last 20 years. Clinically, she takes care of children with inherited and acquired blood disorders. Her research interests lie in studying the genetic therapies for hematopoietic stem cell disorders with a focus on hemoglobinopathies. She has been studying gene transfer into murine and human hematopoietic stem cells (HSCs) using different viral vector platforms such as -retrovirus (RV), lentivirus (LV), adeno-associated virus (AAV) and foamy virus (FV) vectors, mechanisms by which gene transfer affects HSC long term engraftment potential, and translation of genetic therapies for inherited hematological disorders such as XSCID and leukocyte adhesion deficiency, hemophagocytic lympho-histiocytosis, beta-thalassemia and sickle cell anemia (SCA). She initiated lentiviral gene therapy for SCA from the bench to the clinic. More recently, she has embarked on gene editing approaches for genetic therapies of hematopoietic disorders, with a focus on tailoring the choice of DNA-repair after a site-specific break by Cas9, with a goal of enhancing homology directed repair and reducing the error-prone 'end joining' specifically at the Cas9 cut sites. She is currently a Professor of Pediatrics, the Marjorie Johnson Chair of Gene and Cell Therapy, and the Director of the Cincinnati Children's Comprehensive Sickle Cell Center at the Cancer and Blood Disease Institute, Cincinnati Children's' Hospital and University of Cincinnati.

GENE EDITING AND GENE THERAPY

Caterina P. Minniti, M.D.
Professor of Medicine and Pediatrics, *Albert Einstein College of Medicine*
Director, *Sickle Cell Center, Montefiore Medical Center*
Bronx, NY, USA

Dr. Minniti is Professor of Medicine and Pediatrics at Einstein College of Medicine. She is the Director of the Sickle Cell Center for Adults at Montefiore Hospital, whose mission is to provide exceptional, seamless, comprehensive, compassionate and individualized care, education, counseling and research for people living with sickle cell disease. Dr. Minniti is a clinical trial specialist and a translational researcher who believes that the best way to provide care for SCD patients is on a continuum, from birth to adulthood.

The focus of her research is in understanding mechanisms that lead to end organ damage in order to identify early biomarkers and targeted therapies. Her interests have spanned from stroke to pulmonary hypertension and most recently, she has focused on leg ulcers as they represent a window into the vasculopathy in SCD. She aims to develop pathogenetically based therapeutic approaches for preventing and treating SCD-related end organ damage. Before moving to New York, she was a member of the Hematology Branch of the National Institute of Heart Blood and Lung, where she developed a topical treatment for chronic leg ulcers in SCD. She is author of more than 130 peer-reviewed articles and several book chapters. Her contributions have been recognized by the American Society of hematology, as and invited member of the Sickle Cell Disease Clinical Endpoints Workshop in 2019 and by the leadership of NHLBI as an incoming member of the NIH Sickle Cell Disease Advisory Committee in 2019.Dr Minniti has received recognitions from her peers, as Scientific Chair of the 2019 Foundation for Sickle Cell Disease Symposium and form patients organizations, as recipient of the Sickle Cell Thalassemia Patient Network of New York "Distinguished Service Award" in 2018.

LEG ULCERS

Belinda Morrison M.B., B.S., D.M.
Senior Lecturer and Head of the *Division of Urology*
Consultant, *Surgery, University of the West Indies (UWI), Mona*
Supervisor Doctor of Medicine (DM) *Programme in Urology*
Kingston, Jamaica

Dr Belinda Morrison is a Consultant Urologist at the University Hospital of the West Indies, Mona campus, Jamaica. She is currently Lecturer and Head of the Division of Urology at the University of the West Indies. She completed undergraduate and postgraduate training at the University of the West Indies, Mona campus.

Her areas of academic interest include prostate cancer and andrology, where she has published several articles in peer-reviewed journals and book chapters. Dr Morrison has made many local, regional and international presentations to audiences in her field of urology. She is extensively involved in research, particularly as it related to describing the treatment and epidemiology of prostate cancer in Jamaica.

Dr Morrison is a volunteer at the Jamaica Cancer Society where she performs regular monthly prostate screening. In addition, she travels across the island to many churches, public and private organizations and small groups to give men's health talks. Dr Morrison is passionate about health education to the public and regularly engages the media to facilitate this.

She is the current President of the Jamaica Urological Society and member of the Medical Association of Jamaica, American Urological Association and Sexual Medicine Society of North America.

UROLOGY AND SCD

Charles Quinn, M.D., M.S.
Medical Director, *Erythrocyte Diagnostic Laboratory*
Medical Director, *Pediatric Sickle Cell Disease Program*
Professor, *UC Department of Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA*

Dr. Quinn is pediatric hematologist with a clinical focus on sickle cell disease. He is the medical director of the Pediatric Sickle Cell Disease Program and the medical director of the Erythrocyte Diagnostic Laboratory at Cincinnati Children's Hospital. He is also the medical director of the Ohio Department of Health Regional Sickle Cell Services Program (Region 1) for newborn screening follow-up. His current main clinical research interests include the causes and treatments of the cardiac and renal manifestations of sickle cell disease.

EXPERIENCE WITH L-GLUTAMINE

Oxidative stress is an important contributor to the pathophysiology of sickle cell disease (SCD). The pathways involved are complex and interlinked. L-glutamine is an amino acid with myriad roles in the body, including the synthesis of antioxidants, such as reduced glutathione and the cofactors NAD(H) and NADP(H), as well as nitric oxide—so it has therapeutic potential as an antioxidant. However, the relative impact of L-glutamine on the redox environment in red blood cells in SCD is not fully understood, and there are few therapeutic trials of L-glutamine in SCD. Despite the FDA approval of L-glutamine for SCD, more research is needed to understand its proper dosing and clinical effects

Marvin Reid, M.B., B.S., Ph.D.
Director, *Tropical Metabolism Research Unit*
Caribbean Institute for Health Research
The University of the West Indies (UWI), Mona
Kingston, Jamaica

Prof Marvin Reid is the director of the Tropical Metabolism Research Unit, Caribbean Institute for Health Research (CAIHR) and Associate Lecturer in the Department of Community Medicine & Psychiatry at The University of the West Indies, Mona (The UWI). His research interests spans the gamut of community medicine, clinical trials and human metabolism. He has co-authored over 140 peer-reviewed articles and has received the Mona Campus Principal's and The UWI Vice Chancellor's Award for Research Excellence as well as other international awards for research publications. Professor Reid practises as a Family Physician in a group practice, and is a member of the Family Medicine Specialty Board at The UWI which advises on postgraduate Family Medicine training. He is the President of the Caribbean College of Family Physicians (CCFP) and the North American Region of World Organization of Family Doctors as well as a member of several national and international professional bodies including the Medical Association of Jamaica, American Physiological Society and the Research Advisory Committee of Caribbean Public Health Agency (CARPHA).

PEOPLE WITH SCD SHOULD BE PRIMARILY CARED FOR BY HEMATOLOGISTS- NO

Sickle cell disease (SCD) is a hereditary disease in which the inheritance of the gene for haemoglobin S in a homozygous state (Hb SS), or with a gene for another abnormal haemoglobin (eg. Hb SC, SB0, SB+) results in the production of abnormal "sickle-shaped" red blood cells. Abnormal "sickle-shaped" red cells give rise to the characteristic chronic haemolysis and vaso-occlusion associated with the disease. This results in a chronic lifelong condition with unpredictable manifestations as well as an unpredictable clinical course. Sickle cell disease poses a significant public health burden in Jamaica with an incidence of 1 in 150 births.

Traditionally in many jurisdictions, SCD has been the purview of departments of haematology and haemtaologists. The model of care practiced in this setting is often disease driven with focus on the acute manifestations of the disorder. But the reality is that sickle cell disease is a *chronic disease* with manifestations from as early as 4 months in some individuals with overt and subclinical features of chronic organ damage through the life course.

The appreciation that SCD is a chronic disease suggests that quality medical care will need to be delivered using models of care that are appropriate for chronic diseases. The World Health Organization has developed a framework the "Innovative Care for Chronic Disease Framework" which incorporates these principles. Essentially the Framework postulates 3 levels of interactions for the delivery of quality health care to persons with chronic diseases, namely, the micro level, meso level or organizational level and policy level. Within this context, there is an abundance of data that suggests that health systems that are based on

primary health care, deliver better health outcomes, greater public satisfaction at lower costs more equitably. Family Physicians are the physician specialist that such systems revolve around to provide a continuum of care through the life course addressing the physical, psychological, social, and cultural determinants of their client's health needs. With limited haematologist resource of 0.58 per 100,000 in the case of Jamaica compared to the USA 2.2 per 100,000 and with the high financial and infrastructure requirements for disease modifying therapies of chronic blood transfusion, bone marrow transplantation and gene therapies, it makes good policy sense to upscale Family Physicians to manage the common manifestations of SCD in jurisdictions where the burden is high and resources are limited.

A. Parker Ruhl, M.D., M.H.S.
Associate Research Physician, *Laboratory of Malaria and Vector Research*
National Institute of Allergies and Infectious Diseases
Pulmonary Branch, National Heart, Lung, and Blood Institute
National Institutes of Health, Bethesda, MD, USA

Dr. Ruhl completed her training in Pulmonary Medicine at Johns Hopkins Hospital and Critical Care Medicine at the NIH Clinical Center. She is an Associate Research Physician in the Physiology Unit of the Laboratory of Malaria and Vector Research at the National Institute of Allergy and Infectious Diseases and the Pulmonary Branch of the National Heart, Lung, and Blood Institute. Her current research is focused on pulmonary and vascular disease related to sickle cell disease and alpha thalassemia.

RESPIRATORY COMPLICATIONS

Dr. Ruhl will discuss the respiratory complications of sickle cell disease with a focus on 1) acute chest Pulmonary complications of sickle cell disease (SCD) are diverse and encompass acute and chronic disease. The understanding of the natural history of pulmonary complications of SCD is limited, no specific therapies exist, and these complications are a primary cause of morbidity and mortality. Dr. Ruhl will highlight key unanswered questions in several areas of sickle cell lung disease from the recent American Thoracic Society Workshop Report developed by a multidisciplinary group of pediatric and adult hematologists, pulmonologists and emergency medicine physicians.

Vandana Sachdev, M.D.
Director, *Echocardiography Laboratory, Cardiology Branch*
National Heart, Lung, and Blood Institute
National Institutes of Health
Bethesda, MD, USA

Vandana Sachdev is a cardiologist and Staff Clinician in the Cardiology Branch of the NHLBI Division of Intramural Research. She received her M.D. from the University of Michigan and trained in cardiology at the University of Maryland. She joined the NHLBI in 1998 and is now the Director of the Echocardiography Laboratory. She is a member of the American Society of Echocardiography and is active in various

committees and task forces. Dr. Sachdev's lab served as the core lab for the Walk-Phasst study and for other studies supported by NHLBI. Her research area of interest is cardiac imaging and she has worked on phenotyping the sickle cell cohort here as well as numerous other rare disease groups.

CARDIAC COMPLICATIONS OF SICKLE CELL DISEASE

Patients with SCD develop a rheologic cardiomyopathy in which anemia leads to increased plasma volume, elevated cardiac output and dilation of all cardiac chambers. Increased wall stress in the dilated left ventricle can result in compensatory hypertrophy and diastolic dysfunction. Sickled cells become entrapped in the microvasculature leading to ischemia and reperfusion injury in multiple organs, including the heart and lungs. Tricuspid regurgitation velocity, measured by echocardiography, is a powerful predictor of mortality because it functions as an indicator of both cardiac and pulmonary vasculopathy.

Graham Serjeant
Professor Emeritus, *Faculty of Medical Sciences*
University of the West Indies
Kingston, Jamaica

After Clare College, Cambridge, the London Hospital Medical School, and 3 years of postgraduate education, he departed for Jamaica in August 1966 to work in the Department of Medicine, University Hospital of the West Indies, Kingston. He collaborated with Dr. Paul Milner in the Sickle Cell Clinic and was funded by the Wellcome Trust for sickle cell research from 1967-1971. In late 1971, he joined the MRC Abnormal Haemoglobin Unit, Cambridge and in late 1972 returned to Jamaica to work at the MRC Epidemiological Research Unit at the University of the West Indies. From 1973-1981 he established the Cohort Study based on all cases detected during the screening of 100,000 consecutive births. From 1974-1999, he directed the MRC Laboratories at the University of the West Indies continuing studies in the natural history of sickle cell disease. In 1986 the Sickle Cell Trust (Jamaica) was formed as a locally registered charity to raise funds to build a dedicated Sickle Cell Clinic (1987-1988) and the Education Centre for Sickle Cell Disease (1994). Since retiring from the MRC Laboratories in 1999, he continued as Chairman of the Sickle cell Trust developing public education programmes in sickle cell disease among Jamaican secondary schools. From 2007, the Manchester Project in central Jamaica offered free identification of haemoglobin genotypes to over 16,000 senior school children with counselling of carriers. Newborn screening was then set up for 15,000 births in 12 hospitals throughout south and west Jamaica to identify their offspring and to determine whether knowledge of the genotype had reduced the frequency of births affected by sickle cell disease. For the last 30 years, he has collaborated with colleagues on the development of sickle cell services and research in Brazil, Europe, African countries, the Arabian Gulf and increasingly in India. The Jamaican work on sickle cell disease has been recognised by the British Government in 1981 with the award of the CMG (Companion of the Most Distinguished Order of St. Michael and St. George) and by the Jamaican Government with the CD (Order of Distinction, Commander Class) in 1996 and the OJ (Order of Jamaica) in 2015.

BLOOD TRANSFUSION IS UNDER UTILIZED FOR SICKLE-RELATED COMPLICATIONS- NO

Blood transfusion can be life saving in sickle cell disease for complications associated with acutely lowered hemoglobin levels such as in acute splenic sequestration and aplastic crisis. There is also evidence that chronic transfusion may prevent some complications associated with vaso-occlusion such stroke. However, donated blood is a foreign protein which may carry serious risks such as infections and alloimmunization and chronic programs carry the risks of iron overload and maintaining venous access. As with all medical decisions, the use of acute or chronic transfusions must be based on evidence supporting clear benefit of potentially dangerous therapies.

Claire Sharpe, MBBS, PhD
Professor of Renal Medicine
King's College London / King's College Hospital
London, UK

Claire graduated in Medicine from University College London in 1991 and after specializing in Renal Medicine received a Kidney Research UK Clinical Training Fellowship in 1999 to undertake a PhD in renal fibrosis at King's College London under Professor Bruce Hendry. In 2002 she was awarded a Department of Health 5-year Clinician Scientist Intermediate Fellowship and completed her specialist clinical training in 2004. In 2009 she was awarded a NHS/HEFCE Clinical Senior Lectureship allowing her to work as a clinical academic devoting 50% of her time to research and 50% to clinical activity.

Claire's main research interest is in the study of cell signaling pathways in renal fibrosis with a focus on discovering new therapeutic targets.

Claire has been involved in the combined renal and sickle cell clinic at King's College Hospital since it began in 2004. She has developed a strong interest in the underlying mechanisms and management of sickle cell nephropathy and is actively involved in studying both its epidemiology and the outcomes of treatment. The clinic focuses on patient education, early intervention and on-going monitoring with the aim of slowing disease progression and minimizing the number of patients who require renal replacement therapy in the long run.

RENAL COMPLICATIONS

As the life expectancy of patients with sickle cell disease (SCD) continues to improve, the spectrum of complications suffered by these patients has shifted towards chronic disease. Sickle cell nephropathy (SCN) is a well-known complication of the condition which is now recognised to be a much more prevalent problem, particularly in older patients. Early epidemiological studies characterized patients with end-stage renal failure and HBSS disease to be in their early twenties with a life expectancy of less than 30 whereas more recent observational data has suggested that it is becoming increasingly prevalent and a major cause of death in patients over the age of 60. It is therefore important to recognise the early signs of SCN, and other factors which may influence the course of chronic kidney disease, so that we may identify patients who are at risk of developing renal failure and intervene early.

This talk will cover the pathophysiology of sickle cell nephropathy, how to recognise risk factors for developing renal complications, what treatment options are available to prevent progression and how best to manage patients with end-stage kidney disease with dialysis and transplantation. It will be illustrated with examples from our own patient population.

Arun Shet, M.D., Ph.D.
Senior Research Clinician and Clinical Investigator, *Sickle Cell Branch*
National Heart, Lung, and Blood Institute
National Institutes of Health
Bethesda, MD, USA

Dr. Shet is currently a Senior Research Physician and Clinical Investigator at the National Heart Lung and Blood Institute in the Sickle Cell Branch. The main focus of Dr Shets' research is the intersection of inflammation and coagulation on the thrombotic vascular pathobiology of Sickle Cell Disease. Dr. Shets' early research investigated the cellular origin of blood microparticles, with rigorous studies that involved phenotypic characterization and quantification of these subcellular particles. He identified circulating tissue factor positive microparticles and demonstrated their ability to accelerate coagulation in vitro, thus positing a role for vascular coagulation in the clinical manifestations of SCD. He continues to investigate the levels of tissue factor positive vesicles in SCD patients that have had a previous thrombotic event. Currently, he is actively involved in clinical research at the Sickle Cell Branch serving as principal investigator on two active research protocols and associate investigator on four other active research protocols recruiting patients with sickle cell disease.

HOW I MANAGE VENOUS THROMBOEMBOLISMS IN SCD

Sickle cell disease (SCD) is a well-recognized hypercoagulable state and epidemiological studies have quantified the impact of venous thromboembolic disease (VTE) on disease morbidity and mortality. Consequently, an emerging consensus is gathering that the thrombogenic potential for developing recurrent VTE in SCD patients is similar to higher-risk thrombophilia's (e.g. antithrombin or protein C and S deficiency), situations in which long-term anticoagulation is recommended. However, there is some uncertainty regarding the exact duration for which anticoagulation beyond 3 months should be recommended. Moreover, the decision to extend anticoagulation exposure in SCD patients is not trivial as they face an increased risk of bleeding. Whether the hyperactive coagulation system contributes to clinical manifestations of SCD, i.e., whether thrombosis results in or worsens acute vaso-occlusive crises is also uncertain. Trials of anticoagulant and antiplatelet agents in SCD patients have yielded less than favorable results and have therefore cast doubt on the role of thrombosis in SCD. Besides, prospective trials specifically evaluating anticoagulation for VTE treatment and prevention in SCD are lacking. Using a case based approach, I will discuss the management of venous thromboembolism in patients with SCD.

Rosalyn Stewart, M.B.A., M.D., M.S.
Director, *Johns Hopkins After Care Clinic*
Johns Hopkins Outpatient Center
Associate Professor of Medicine
Baltimore, MD, USA

Dr. Rosalyn Stewart is Director of Care Coordination and Resource management at The Johns Hopkins Hospital and Associate professor at Johns Hopkins University School of Medicine with joint appointments in the Departments of Internal Medicine and Pediatrics, School of Nursing and Bloomberg School of Public Health. Dr. Stewart coordinates quality improvement efforts geared toward refining health care services and improving the health status of populations. Dr. Stewart's background in preventive medicine and business aspects of health care and health policy coupled with expertise in urban health, health disparities, cultural competency makes her uniquely qualified to lead clinical innovations directed to obviate social determinants of health. She focuses on the combination of sciences, skills and beliefs that center on the maintenance and improvement of health, prevention of disease or future sequelae, examination health of populations in communities rather than individual patients, particularly vulnerable or underserved patients with sickle cell disease. She focuses on skills to succeed in complex health care environments and in creating and maintaining health systems. She has attained the knowledge necessary to understand, analyze, and create innovative medical-delivery systems. Her work has led to the development of innovative team-based comprehensive care that includes use community partners as part of multi-disciplinary care that emphasizes collaboration and utilizes social workers, educators, advanced practice providers, and community health workers in an environment that promotes education and discovery.

EDUCATION OF HEALTH CARE PROFESSIONALS- ECHO

Background

Sickle cell disease is a rare inheritable blood disorder affecting around 100,000 individuals in the U.S[1]. Among many of the challenges faced by individuals living with sickle cell disease is the lack of access to quality care due to a lack of providers with the knowledge necessary to provide quality sickle cell care[2]. In response to this barrier to quality care, Johns Hopkins School of Medicine began hosting a telementoring series to promote and educate participating providers on guideline-based care in sickle cell disease in September of 2015. The Sickle Cell TeleECHO® Clinical Conference Series, hosted weekly, utilizes the ECHO® model of video telementoring that is structured by interactive case-based learning coupled with short didactics. This telementoring model was developed by Dr. Sanjeev Aurora at the University of New Mexico in 2003 to de-monopolize medical knowledge and has since been widely used for telementoring on a variety of topics within the medical field and beyond.

Objective

The primary objective of this activity was to increase the knowledge of providers and promote the use of guideline-based care in treating sickle cell disease with telementoring sessions.

Methods

Data was collected on attendance and provider-reported confidence in treating different aspects of sickle cell care. Electronic surveys were distributed via email invitation between September 2015 and June 2019. The sign test was used to compare the differences in median self-reported likert scale confidence in abilities before and after participating in an ECHO®session. STATA IC 15 was used to perform the analyses and Tableau Public was used for data visualizations.

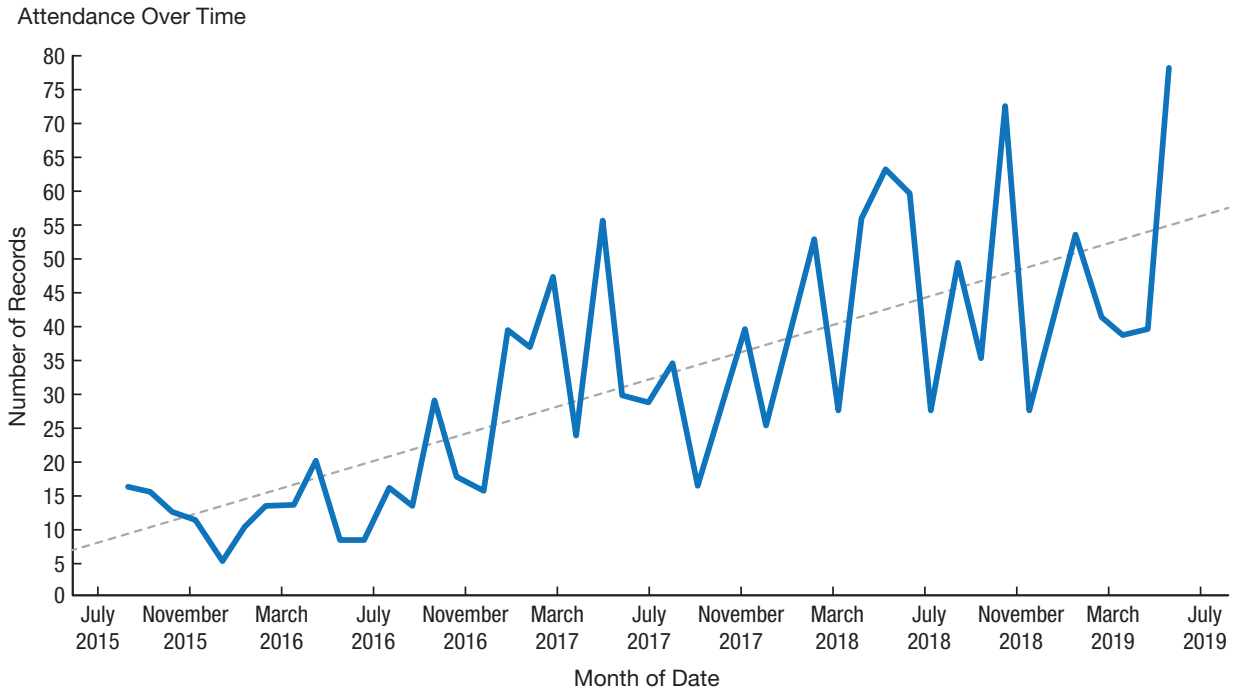
Results

Since inception on September 9th, 2015, 244 unique participants have joined at least one Sickle Cell ECHO® session. Sixty percent of these attendees have been physicians (n=111) and physician assistants or nurse practitioners (n=33). The remaining attendees consist of nurses, social workers, pharmacists, community health workers or patient navigators, other medical staff, researchers, administrators, and insurance representatives. Geographic distribution of participants spans the United States and the Caribbean. A higher concentration of attendees are geographically located in the Northeastern United States, which is expected due to the project's focus on this region.

Over the life of the ECHO® series, 246 unique patients have been presented and guideline-based case recommendations given. Since inception, physician attendance averages 6.1 sessions and physician assistants and nurse practitioner attendance averages 9.8 sessions. Overall attendance continues to grow year after year with average of 5.3 attendees per session in 2015, 5.1 attendees per session in 2016, 9.2 attendees per session in 2017, 13.6 attendees per session in 2018, and 14.1 attendees per session in 2019.

Of a sample of 22 attendees, there was a statistically significant positive change in the median self-reported confidence in managing specific aspects of sickle cell care including: recognizing acute chest syndrome, recognizing the indications for Hydroxyurea, initiating Hydroxyurea management, titrating Hydroxyurea dosing, manage chronic pain in patients with sickle cell disease, manage acute pain in patients with sickle cell disease.

Additionally, in a sample of 18 attendees, 67% reported that they will change their practice as a result of attending the ECHO® session(s).



Conclusion

The increasing utilization and positive provider perceptions of an increase in confidence in managing different aspects of sickle cell care both indicate that the Johns Hopkins Sickle Cell teleECHO® Clinical Conference Series is a useful tool for providers seeing sickle cell patients. Participation in this type of telementoring activity may increase provider knowledge in the treatment of sickle cell disease and the quality of care received by individuals living with the disease. More research is appropriate to test this and explore what aspects of the ECHO® sessions are most attractive to providers.

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Swee Lay Thein, M.B., B.S., F.R.C.P., F.R.C.Path., D.Sc.
Chief, *Sickle Cell Branch*
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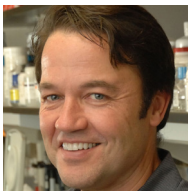
Swee Lay Thein is a hematologist and clinical investigator with more than 30 years of clinical and translational hematology research and extensive personal experience in laboratory research – molecular biology, genetics and genomics. Dr Thein joined the National Heart, Lung and Blood Institute / NIH in spring 2015 asSenior Investigator and Chief of the Institute's Sickle Cell Branch. Prior to this, she was Professor of Molecular Hematology and consultant hematologist at King's College London (KCL), where she served as clinical director of the Red Cell Centre in King's College Hospital. At the hospital, she was involved in the care of adults with sickle cell disease and other red blood cell disorders, and also provided a comprehensive diagnostic service for red blood disorders including antenatal and newborn screening, and prenatal diagnosis of the hemoglobin disorders.

Swee Lay Thein completed her specialist training in general medicine and hematology at the U.K. Royal Postgraduate Medical School, Hammersmith, and the Royal Free Hospital, London. She has also worked in Oxford at the Weatherall Institute of Molecular Medicine (Medical Research Council Molecular Hematology Unit) where she held various positions, including MRC clinical training fellow, Wellcome Senior Fellow in Clinical Science, senior MRC clinical scientist, and the John Radcliffe Hospital as honorary consultant hematologist before she moved to KCL, London, in 2000.

Dr. Thein runs a program on Sickle cell genetics and pathophysiology with an objective of identifying plasma and genetic markers to allow early detection and monitoring of severe complications. Using the hemoglobinopathies as genetic models, her research has contributed significantly to the understanding of genetic modifiers and complex traits and DNA diagnostics in hemoglobinopathies, and unravelling the loci contributing to the control of fetal hemoglobin, a major ameliorating factor in these disorders.

Since 2006, she has directed and hosted an annual 2-day international conference in sickle cell disease, in KCL (London) and the NHLBI/NIH. She has also been previously involved in planning and organising various educational meetings (national and international) and working with the European School of Hematology and European Hematology Association. She was elected to the Fellowship of the UKs Academy of Medical Sciences in 2003.

PEOPLE WITH SCD SHOULD BE PRIMARILY CARED FOR BY HEMATOLOGISTS- YES



John Tisdale, M.D.
Chief, *Cellular and Molecular Therapeutics Branch*
Director, Sickle Cell Program
National Heart, Lung, and Blood Institute,
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John Tisdale received his medical degree from the Medical University of South Carolina in Charleston after obtaining his B.A. in Chemistry from the College of Charleston. He completed an internal medicine and chief residency at Vanderbilt University Medical Center in Nashville and then trained in hematology in the Hematology Branch, National Heart, Lung and Blood Institute (NHLBI), where he served as a postdoctoral fellow. He joined the Molecular and Clinical Hematology Branch of NHLBI in 1998 and is now the Chief of the Cellular and Molecular Therapeutics Branch. In 2011 the College of Charleston recognized Dr. Tisdale with the Alumni of the Year Award and the Pre-Medical Society's Outstanding Service Award in Medicine. He was recently elected to the American Society for Clinical Investigation and is a member of the American Society of Hematology. Dr. Tisdale's research and clinical work center on sickle cell disease.His group focuses on developing curative strategies for sickle cell disease through transplantation of allogeneic or genetically modified autologous bone marrow stem cells.

SOURCE OF CELLS- IMPACT ON SUCCESS OF BMT

Hematopoietic stem cell (HSC) gene therapy has long been pursued as a one-time cure for sickle cell disease (SCD) and viral vector technology has improved such that this long-sought goal is within reach. However, collection of mobilized peripheral blood after G-CSF mobilization, the preferred method for HSC collection, is associated with morbidity and mortality in SCD, leaving steady state bone marrow as the default HSC source for gene therapy applications. We thus investigated the safety and feasibility of peripheral blood (PB) mobilization with plerixafor which unlike G-CSF, act within hours to mobilize HSCs unlike the 5 days of treatment necessary with standard mobilization. We have completed the largest study to date that demonstrates consistent, safe, and sufficient PB HSC collection and processing after plerixafor mobilization. Our results demonstrate that plerixafor mobilized HSCs in SCD are more highly enriched in CD34-bright HSCs compared to steady state SCD bone marrow (BM). In a parallel study, plerixafor mobilized peripheral blood provided higher yields for genetic manipulation. These accumulating data suggest that plerixafor mobilization as the optimal method for HSC collection from patients with SCD.

Marsha J. Treadwell, Ph.D.
Professor of Psychiatry and Pediatrics, *UCSF School of Medicine*
UCSF Benioff Children's Hospital Oakland
Oakland, CA, USA

Dr. Treadwell is a graduate of the University of Washington, with a degree in clinical child psychology. She has spent her professional career at UCSF Benioff Children's Hospital Oakland, specializing in helping children and families cope with the stress of living with medical conditions and treatments. Early in her

career she met young adults with sickle cell disease, who impressed her with their resiliency in the face of excruciating painful episodes, repeated hospitalizations, and potentially shortened lifespans. Dr. Treadwell eventually devoted her career to clinical care, research and community advocacy for individuals with sickle cell disease and their families. She is the Director of the NHLBI funded Sickle Cell Care Coordination Initiative in northern California, that brings together adolescents and adults with sickle cell disease, healthcare providers, policymakers and researchers, to address the longstanding and pervasive health disparities that characterize sickle cell disease care throughout the U.S.

Dr. Treadwell is also Regional Director for the HRSA funded Pacific Sickle Cell Regional Collaborative, a consortium across 13 western states that seeks to improve access to knowledgeable care for individuals with sickle cell disease of all ages. Dr. Treadwell is Adjunct Professor in the UCSF School of Medicine and Jordan Fund Endowed Chair at UCSF Benioff Children's Hospital Oakland. She is recognized for her research that integrates physical, behavioral and psychological processes and has participated in and led numerous research projects, in the U.S., the U.K., Brazil and across the African continent. Dr. Treadwell's goal is to engage multiple sectors of the community to improve the quality of life and quality of care for sickle cell disease. In addition, she mentors high school students through junior faculty, to support their success and to insure that they recognize the importance of keeping issues of diversity, equity and inclusion in the forefront of their clinical and scientific practice.

PSYCHOLOGY IN SCD

Russell Ware, M.D., Ph.D.
Director, *Division of Hematology*
Co-Director, *Cancer and Blood Diseases Institute*
Director, *Global Health Center*
Professor, *UC Department of Pediatrics*
Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

Russell Ware, MD, PhD, has been involved with a wide variety of clinical and translational hematology research projects for over 25 years, but his primary interests have focused on sickle cell disease. Dr. Ware has substantial personal experience with directing patient-oriented research, and he currently runs an NIH-funded laboratory effort that investigates genetic modifiers of sickle cell disease. The main focus of his lab research is to understand the phenotypic variability that occurs with hydroxyurea treatment, through the study of hydroxyurea pharmacokinetics, pharmacodynamics, pharmacogenetics, and pharmacogenomics. Dr. Ware is also the national principal investigator for several NIH-funded multicenter sickle cell clinical trials, including the recently completed Stroke With Transfusions Changing to Hydroxyurea (SWiTCH), and the current TCD With Transfusions Changing to Hydroxyurea (TWiTCH) and Sparing Conversion to Abnormal TCD Elevations (SCATE) studies that include non-US clinical sites. Most recently, Dr. Ware has moved his research efforts into the international arena, starting SCD pilot screening programs in Angola, and now conducting clinical trials to determine the safety and efficacy of hydroxyurea in developing countries.

National Institutes of Health